

Alcohol-related and hepatocellular cancer deaths by country of birth in England and Wales: analysis of mortality and census data

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ABSTRACT

Background The incidence of and mortality from alcohol-related conditions, liver disease and hepatocellular cancer (HCC) are increasing in the UK. We compared mortality rates by country of birth to explore potential inequalities and inform clinical and preventive care.

Design Analysis of mortality for people aged 20 years and over using the 2001 Census data and death data from 1999 and 2001–2003.

Setting England and Wales.

Main outcome measures Standardized mortality ratios (SMRs) for alcohol-related deaths and HCC.

Results Mortality from alcohol-related deaths (20 502 deaths) was particularly high for people born in Ireland (SMR for men [M]: 236, 95% confidence interval [CI]: 219–254; SMR for women [F]: 212, 95% CI: 191–235) and Scotland (SMR-M: 187, CI: 173–213; SMR-F 182, CI: 163–205) and men born in India (SMR-M: 161, CI: 144–181). Low alcohol-related mortality was found in women born in other countries and men born in Bangladesh, Middle East, West Africa, Pakistan, China and Hong Kong, and the West Indies. Similar mortality patterns were observed by country of birth for alcoholic liver disease and other liver diseases. Mortality from HCC (8266 deaths) was particularly high for people born in Bangladesh (SMR-M: 523, CI: 380–701; SMR-F: 319, CI: 146–605), China and Hong Kong (SMR-M: 492, CI: 168–667; SMR-F: 323, CI: 184–524), West Africa (SMR-M: 440, CI: 308–609; SMR-F: 319, CI: 165–557) and Pakistan (SMR-M: 216, CI: 113–287; SMR-F: 215, CI: 133–319).

Conclusions These findings show persistent differences in mortality by country of birth for both alcohol-related and HCC deaths and have important clinical and public health implications. New policy, research and practical action are required to address these differences.

Keywords cirrhosis, epidemiology, ethnicity, liver cancer, mortality

Introduction

Overall, 4% of the global burden of disease is attributable to alcohol, accounting for approximately as much death and disability globally as tobacco and hypertension.¹ Besides causing poor health and premature death mediated through both liver disease and other pathologies, alcohol misuse is now estimated to cost £20 billion a year in England alone.^{2,3} Studies in both Europe and the USA have demonstrated a strong association between alcohol consumption and liver cirrhosis mortality, leading to public health measures to limit the availability of alcohol.^{4,5} Excess consumption increases mortality directly by a number of other mechanisms, increasing the risk of a number of conditions, such as

cardiomyopathy, neuropathy and mental disorders. It also contributes to an increased risk of certain cancers, stroke and external causes of death (such as suicides, accidents and sudden deaths). The Office for National Statistics (ONS) definition of alcohol-related deaths, which includes causes

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Table 1 Office for National Statistics definition of alcohol-related deaths (using ICD-10)

F10	Mental and behavioural disorders due to use of alcohol
G31.2	Degeneration of nervous system due to alcohol
G62.1	Alcoholic polyneuropathy
I42.6	Alcoholic cardiomyopathy
K29.2	Alcoholic gastritis
K70	Alcoholic liver disease
K73	Chronic hepatitis, not elsewhere classified
K74	Fibrosis and cirrhosis of the liver (excluding K74.3–K74.5 – biliary cirrhosis)
K86.0	Alcohol-induced chronic pancreatitis
X45	Accidental poisoning by and exposure to alcohol
X65	Intentional self-poisoning by and exposure to alcohol
Y15	Poisoning by and exposure to alcohol, undetermined extent

regarded as most directly due to alcohol consumption, was devised to help address the multiple influences of alcohol on mortality (Table 1).

In addition to excessive alcohol consumption, chronic viral hepatitis and non-alcoholic fatty liver disease (NAFLD) are other significant aetiological factors for cirrhosis. Approximately 200 000 people in the UK are infected with each of the hepatitis B and C viruses and a substantial proportion have chronic liver disease and its complications.⁶ NAFLD prevalence is found in 17–30% of unselected populations and the prevalence appears to be rising in association with the current ‘obesity’ epidemic.⁷ Regardless of aetiology, one of the major complications of liver cirrhosis is hepatocellular cancer (HCC), the incidence of which has increased over recent decades in the UK.⁸ HCC largely occurs within an established background of chronic liver disease and cirrhosis, and it is the third most common cause of cancer mortality worldwide.⁹

Previous studies in the USA have shown that ethnicity is significantly associated with both alcohol-reported death and liver cirrhosis mortality, with increases in Black and Hispanic groups compared with the White population.^{5,10} In England and Wales, ethnicity is not recorded on death certificates but both all-cause and cause-specific mortality for various conditions has been shown to vary by country of birth.^{11–16} Work by Haworth and colleagues using data collected around the time of the 1991 Census showed a number of significant variations in mortality by country of birth for both liver cirrhosis and HCC.¹⁷ There was a statistically significant 2-fold excess of mortality from liver cirrhosis among men and women born in Scotland and Ireland and men born in East Africa, India and Bangladesh compared with the general population of England and Wales. Higher HCC mortality was reported amongst men

and women born in Bangladesh, the Caribbean and the African Commonwealth.

We provide updated information on alcohol-related and HCC mortality in England and Wales by the country of birth. Information from such analyses is vital for current debate and controversy on the burden and implications of rising mortality from liver diseases, and for subsequent health needs assessment, policy formulation, and equitable clinical and preventative care delivery.¹⁵

Subjects and methods

Mortality data

Mortality data for the years 1999 and 2001–2003 by age, sex, country of birth and underlying cause of death were analysed at the ONS for residents of England and Wales at the ONS. The analysis used data coded according to the International Classification of Diseases, tenth revision (ICD-10; World Health Organization, 1992)—data for the year 2000 were not included as they were only coded using the ninth revision (ICD-9). We included countries, or groups of countries, if there were over 1000 deaths from all causes among adults (>20 years of age) born in each country or group of countries. ICD-10 codes were used as follows: alcohol-related deaths (Table 1, F10, G31.2, G62.1, I42.6, K29.2, K70, K73, K74 [excluding K74.3–K74.5], K86.0, X45, X65 and Y15) and hepatocellular carcinoma (C22). Data for mortality from alcoholic liver disease (K70) and other liver diseases (K71–76) are also available and are included in online Supplementary Material.

Population data

Population data by age, sex and country of birth were obtained from the 2001 Census of England and Wales. Place of birth was categorized by the individual country (Scotland, India, Bangladesh, Pakistan, China and Hong Kong), the combinations of England and Wales and the Republic of Ireland and Northern Ireland or country group (East Africa, Eastern Europe, Middle East, North Africa, West Africa, the West Indies), as in previous studies.¹⁴

Statistical analysis

Indirect standardization was used to adjust for differences in age distribution between the populations of interest. Cause-specific mortality data for England and Wales as a whole in 1999 and 2001–2003 by sex and 5-year age group were used as the standard. Conventional methods were used to estimate standardized mortality ratios (SMRs) and 95%

confidence intervals (CI) by the country of birth for men and women aged 20 years and over.¹⁶

Presentation of results

With indirect standardisation, each country of birth group can be compared with the whole England and Wales population (i.e., SMR = 100). Comparisons can be made by gender separately (i.e., the ratios for men are only comparable with other men, and women with other women).

As people born in England and Wales form most of the study population, SMRs for this group tend to be close to 100, indicating little difference from the population as a whole. However, as a consequence of the large numbers of deaths among people born in England and Wales, small differences tend to be statistically significant even when they are unlikely to be clinically relevant. Therefore, no further comment is made on the findings for people born in England and Wales, as in previous analyses.¹⁴

Results

Populations studied

The total of the sub-populations included in this study represent 99.5% of the adults aged 20 years or older

enumerated in the 2001 Census of England and Wales. Age structures differed between sub-populations, with individuals from Bangladesh and West Africa having relatively young populations, reflected by larger proportions of people in the 20–44-year age group.

Mortality from alcohol-related conditions

There were 20 502 alcohol-related deaths in England and Wales in the study (Fig. 1 and online Supplementary Material Table S1). SMRs were raised in men born in Ireland, Scotland and India and in women born in Ireland and Scotland. SMRs were lower than the national average for men and women born in Bangladesh, Middle East, West Africa, Pakistan, China and Hong Kong, the West Indies and East Africa and for women born in North Africa and India. There were 13 982 deaths from alcoholic liver disease and 10 461 deaths from other liver diseases in England and Wales in the study period (online Supplementary Material Tables S2 and S3 and Figs S1 and S2).

Mortality from HCC

There were 8266 deaths from HCC in England and Wales (Fig. 2 and online Supplementary Material Table S4). SMRs for HCC were above the national average in men and

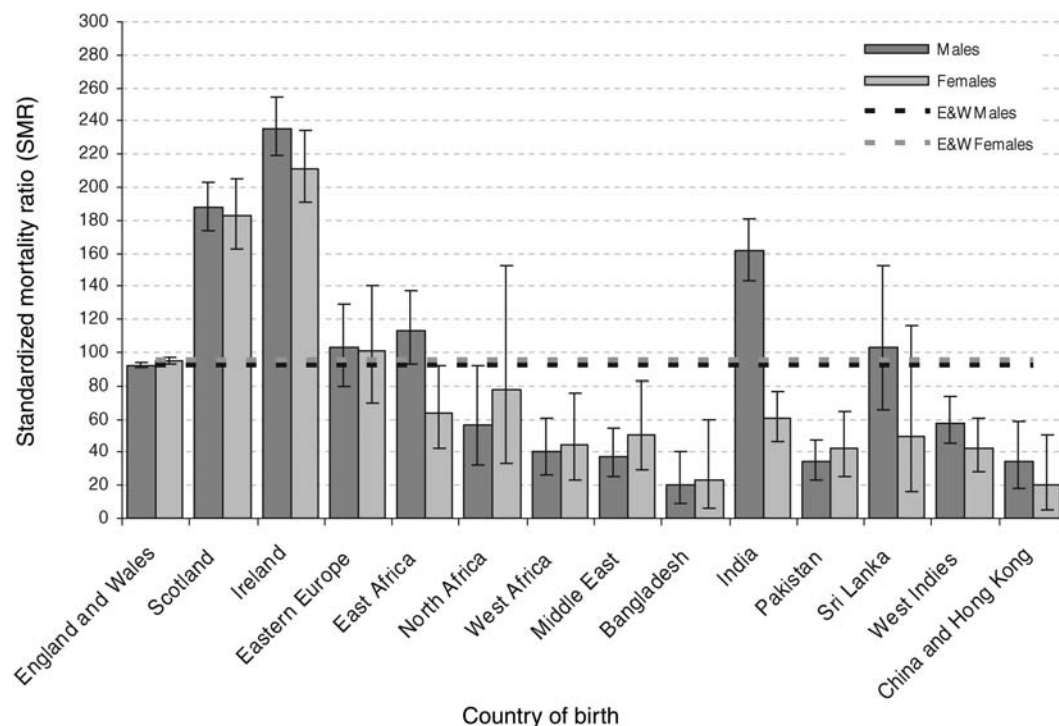


Fig. 1 Standardized mortality ratios (SMRs) for alcohol-related deaths by sex aged 20 years and over and country of birth, England and Wales (E&W), in 1999 and 2001–2003.

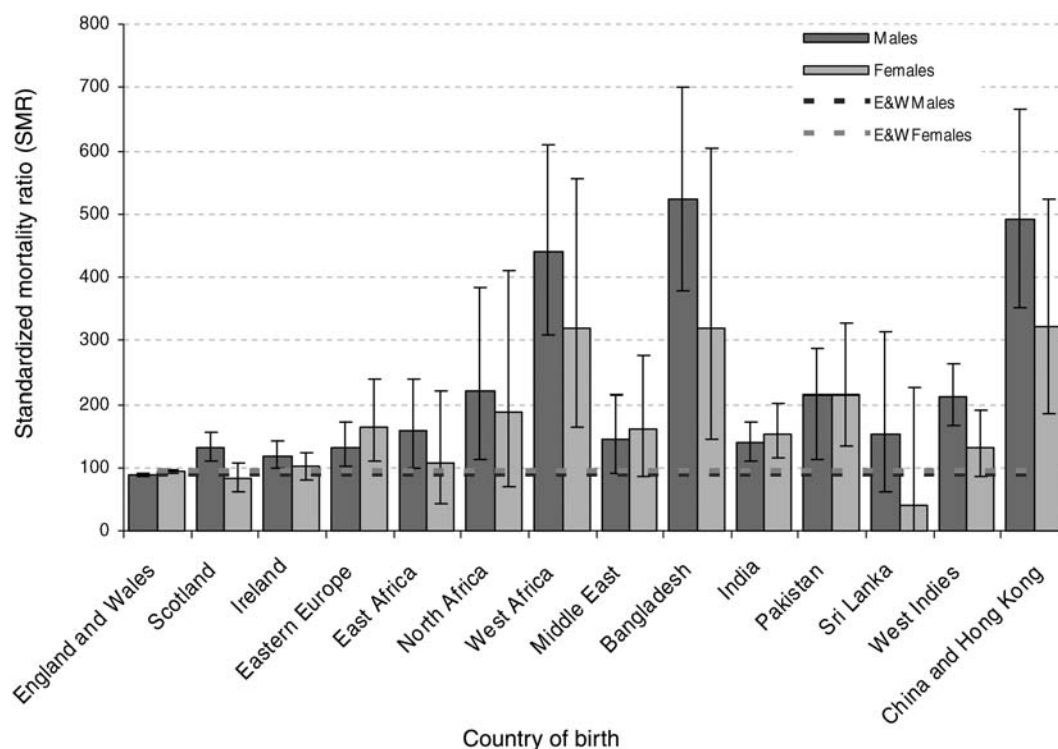


Fig. 2 Standardized mortality ratios (SMRs) for hepatocellular cancer (HCC) deaths by sex aged 20 years and over and country of birth, England and Wales (E&W), in 1999 and 2001–2003.

women born in Bangladesh, China and Hong Kong, West Africa and Pakistan. SMRs for men born in the West Indies and North Africa were also higher than the national average. No SMRs for HCC were statistically significantly below the national average.

Discussion

Main findings of this study

There were important inequalities in mortality ratios from alcohol-related causes and HCC by country of birth in England and Wales, with similarities and differences from those reported previously, which may relate to the different definitions of disease.¹⁷ The high alcohol-related mortality in men and women born in Scotland and Ireland and men born in India are of concern, given the potential for prevention. Alcohol-related mortality in people born in countries where abstinence is more common, such as parts of Asia and Africa, was lower than the average in England and Wales, especially in women.

Mortality from HCC was higher than the national average in men and women born in Bangladesh, China and Hong Kong, West Africa and Pakistan. Although the numbers of deaths are small for each country of birth group, the differences in HCC mortality are unlikely to be artefactual.¹⁷

What is already known on this topic

Definition of alcohol-related mortality

The definition of death from alcohol-related conditions has changed over time.¹⁸ It consists of a heterogeneous mix of conditions, but the most common is alcoholic liver disease (in this time period, 61 and 57% of alcohol-related deaths for men and women, respectively). As this definition does not include other diseases where alcohol has some causal relationship, such as oral or oesophageal cancer, accidents and sudden deaths, the burden of alcohol-related mortality is underestimated. This definition allows for comparisons of mortality from conditions most definitively associated with alcohol consumption.

The pattern of mortality from other liver diseases by country of birth is very similar to that of alcoholic liver disease, because 40–67% of deaths from unspecified liver disease are attributable to heavy alcohol consumption.^{19,20}

Other liver diseases comprise a heterogeneous group of conditions, including viral hepatitis, non-alcoholic fatty liver disease (NAFLD), primary biliary cirrhosis, haemochromatosis, autoimmune hepatitis, Wilson's disease and alpha 1 anti-trypsin deficiency. Primary biliary cirrhosis accounted for only 554 deaths among women (11.8%) in the identified time period, making its overall contribution small in comparison with alcohol. The other autoimmune liver diseases,

haemochromatosis, Wilson's disease and alpha 1 anti-trypsin deficiency, are not identified on the ICD coding, and so their contribution to overall liver cirrhosis mortality and the effect of country of birth cannot be assessed.

Causes of variations in alcohol-related mortality

Many of the underlying reasons for susceptibility to liver disease remain unknown, but there is undoubtedly a genetic component as well as an effect of environmental factors, such as alcohol intake and viral infections.²¹ An example of how the two interrelate, is the fact that about half of all Chinese people have a deficiency of the low-Km aldehyde dehydrogenase (ALDH2) isoenzyme, resulting from inheritance of a mutant ALDH2*2 allele.²² This is likely to inhibit alcohol consumption. Inequalities by race occur in treatment access and outcome, for example, in liver transplantation in the USA, but it is not known if this occurs in the UK.²³ Socioeconomic status may be a potential confounding factor. Education has also been shown to magnify ethnic variation in alcohol-related problems in the USA.²⁴ Some of the differences we have demonstrated might reflect variations in socioeconomic status between the groups compared, but the corresponding national statistics are not available for adjustment.

Differences in alcohol consumption by country of birth (ethnicity) and sex are the likely major causes of the inequalities in alcohol-related mortality demonstrated. In the Health Survey for England and Wales in 2004, men born in Ireland were more likely to drink at high-risk levels and experience drinking problems than non-Irish men. Although data for Scottish people in England and Wales are not available, in the Scottish Health Survey of 2003, alcohol consumption was even higher for Scottish men and women. High hospital admission rates for alcohol-related mortality in Scottish and Irish people, compared with the general population in London, was described more than 20 years ago.²⁵ More recently, the analysis of routine mortality statistics demonstrated a stark increase in liver cirrhosis mortality in Scotland compared with the rest of Europe.⁴

All non-White minority ethnic groups were less likely than the general population to consume alcohol in excess of the daily guidelines (Fig. 3) with marked gender differences. In the West Midlands, South Asian men (of whom 80% were estimated to be Sikh) had an SMR for alcoholic liver disease deaths of 379 compared with the general population (100).²⁶ Our study does not support that level of excess. However, south Asians are a heterogeneous group: alcohol consumption is higher in Sikhs than in Hindus and (often abstinent) Muslims, with heavy spirit drinking especially common among Sikh men.²⁷ This heterogeneity may

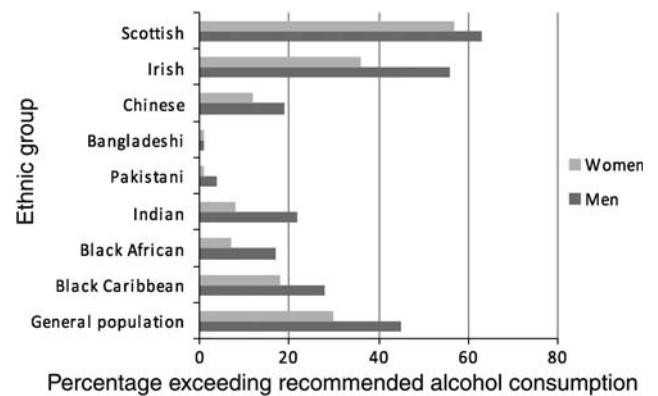


Fig. 3 Adults drinking above recommended alcohol consumption (four units for men, three units for women) on heaviest drinking day by ethnic group and sex; adults aged 16 years and over. Sources: Department of Health (2005), Health Survey for England 2004. The Information Centre: London and Scottish Executive (2004), Scottish Health Survey 2003.

disguise high alcohol consumption in some populations of Indian origin.

Apart from alcohol, the major causal agents for liver disease are chronic viral hepatitis and NAFLD. In an Italian case control study, the population attributable risk for cirrhosis was estimated to be 68%, with the remainder almost entirely due to chronic viral hepatitis.²⁸ The apparently low risk of mortality from other liver diseases in men born in China and Hong Kong, a group in which higher mortality rates secondary to hepatitis B virus might have been expected, may be artefactual due to the small numbers of deaths, or the inclusion of lower risk White populations born there. There are no current estimates of the attributable risk of cirrhosis due to obesity and NAFLD, but there may be a synergistic effect of fatty liver with alcohol and viral hepatitis on the risk of cirrhosis and HCC.²⁹ South Asian and Hispanic populations are more likely than European populations to have central obesity, insulin resistance and the metabolic syndrome phenotype, which may increase their risk of NAFLD and consequent liver disease mortality.^{30,31} Effectively, raised mortality from liver diseases could result from excessive alcohol intake, NAFLD, chronic viral hepatitis or a combined effect of these factors.^{7,8,29–31} Further work on the relative importance of these putative factors in different population groups is required.

Nonetheless, alcohol-related mortality in the UK has increased each year in the decade prior to 2006 but did not rise in 2007.³² Globally, it has recently been reported that countries that previously had a reputation for lower levels of alcohol intake, such as India, also have increasing rates of alcohol-related disease, with resultant major public health consequences.³³

Hepatocellular carcinoma

HCC mortality had a different pattern by country of birth to that of alcohol-related disease and is the highest in those regions where chronic viral hepatitis is endemic. In the USA, age- and sex-adjusted rates of HCC are as high in Asians as in African-Americans; both are approximately double that in the rest of the population.³⁴ The likely reason for this ethnic variability includes differences in the prevalence and acquisition time of major risk factors in underlying liver diseases. Other factors may be synergistic, for example, HCC risk increased in a linear fashion amongst alcohol drinkers consuming above 60 g daily, with a further 2-fold increase in those with concomitant hepatitis C virus infection.³⁵ Previous population-based studies have also demonstrated that obesity and diabetes are independent risk factors for HCC.^{9,35} Although there are case reports of non-alcoholic steatohepatitis (which occurs when inflammation develops in addition to NAFLD) leading to HCC, chronic viral hepatitis or alcohol appear to play a more important role at present.^{9,35}

What this study adds

Many of the alcohol-related and liver disease mortality patterns we have demonstrated are similar to those reported around the 1991 Census.¹⁷ What has changed? There has been some reduction in the extent of the inequalities, though these still remain very large; however, consumption of alcohol has risen, the population prevalence of hepatitis B has risen and central obesity has become much more common.^{6,7} Previous recommendations, including hepatitis B vaccination for high-risk country of birth/ethnic groups for prevention of subsequent HCC, continue to be relevant.¹⁷ The major public health approach to prevent cirrhosis at a population level is reducing alcohol consumption. Strategies to reduce the prevalence of obesity and viral hepatitis could also contribute to a reduction in liver disease.

The public health significance of alcohol consumption is underestimated from under-reporting of alcohol-related disease and its secondary role in external mortality, such as road traffic accidents, which are not included in these analyses. Although based in England and Wales, this study may have policy implications for other similar countries. Sustaining low mortality rates for alcohol-related causes for people born outside England, Scotland and Ireland (and men in India) provides a public health challenge, and could inform policy development as well as direct the definition of targets. In contrast to previous findings, the SMR for alcohol-related deaths for Bangladeshi men was not elevated, as predictable on known alcohol behaviour.¹⁷ The explanation for this apparent discrepancy is not known but may be a previous data artefact.

The role of immunization, screening and appropriate treatment of viral hepatitis in order to combat the high rates of HCC in men and women from a number of countries, including Bangladesh, China and Hong Kong, West Africa and Pakistan, definitely requires attention. Given persisting inequalities,¹⁷ a case-finding approach by ethnicity may be the rational approach for HCC screening, treatment and prevention.

Limitations and strengths of the study

Potential sources of bias in these estimates include errors in population estimates, return migration, numerator–denominator bias (e.g. when country of birth for an individual is recorded differently in the Census and on a death certificate, implying misclassification in one or the other) and inaccurate reporting of the cause of death.¹⁵ The fact that SMRs are not consistently high or low for both alcohol-related mortality and hepatocellular carcinoma suggests that such systematic biases are not substantial. The low numbers of deaths for people born in some countries may mean that some differences of clinical importance may not be identified as being statistically significant. Variation in the accuracy of the cause of death described on death certificates by country of birth may exist,¹⁵ which may be especially significant for alcohol-related mortality because of social stigma.¹⁰ However, the definition of alcohol-related death includes all liver cirrhosis regardless of whether or not alcohol was specifically mentioned on the death certificate.

Data are currently lacking in populations from countries from which migration to England and Wales has taken place more recently, such as Eastern Europe (where alcohol already accounts for a high proportion of premature mortality).³⁶ Country of birth cannot be used to identify the children of immigrants and we were not able to make comparisons between mortality data for migrants to England and Wales and their countries of birth (due to a lack of comparable and reliable data). However, these limitations are unlikely to wholly, or even largely, explain the substantial variations found here. Our analysis is of a comprehensive national data set and corroborates other analyses.^{12,13,17} The validity of the country of birth as a proxy for ethnicity varies within and between populations; although similar patterns by ethnicity are likely, we need new methods and data to establish this.^{37,38}

A note on terminology relating to ethnicity

There is no consensus on appropriate terms for the scientific study of health by ethnicity, and published guidelines are

yet to be widely adopted. We have followed general conventions used in the UK and, whenever appropriate, the terminology used by the original authors. For example, in the UK the term ethnic minority group usually refers to minority populations of non-European origin and characterized by their non-white status (we use it this way). The term South Asian refers to populations originating from the Indian Sub-continent, effectively, India, Pakistan, Bangladesh and Sri Lanka. White is the term currently used to describe people with European ancestral origins. By ethnicity we mean the group a person belongs to as a result of a mix of cultural factors including language, diet, religion and ancestry. In this work, country of birth is used as a proxy for ethnicity.³⁹

Author contributions

Details of contributors and the name of the guarantor: N.B., S.W. and R.B. designed and conceived the study, with assistance from C.G. and A.B. Analyses were carried out by C.G. and A.B., with interpretation by N.B., S.W. and R.B. The manuscript was written by N.B., S.W. and R.B., with final approval from all authors. S.W. is the guarantor.

Supplementary data

Supplementary data are available at the *Journal of Public Health* online.

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